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BACON & THOMAS, PLLC
625 SLATERS LANE
FOURTH FLOOR
ALEXANDRIA, VA 22314-1176

EXAMINER	
LUM, LEON YUN BON	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,232	MANSSON ET AL.	
	Examiner	Art Unit	
	Leon Y. Lum	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 17-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 17-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/22/06, 11/28/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicants' election with traverse of Group 1, claims 1-9 and 16 in the reply filed on November 28, 2008 is acknowledged. The traversal is on the ground(s) that the elected claims, together with claims 17-24 (newly added), form the same inventive concept and are linked to each other. *See* page 6, second paragraph of the reply. Moreover, Applicants argue that the amendment inserting the term "unlabelled" in claim 1 negates the Brosnan reference as rendering the elected claims free of the prior art. With this argument in mind and due to the cancellation of claims 7-15 and the content of newly added claims 17-24, the restriction requirement set forth in the previous Office Action is now withdrawn.

Applicants' election of narcotics (claim 6) with traverse is acknowledged. *See* reply, page 8, second paragraph. The traversal is on the grounds that the various species are not patentably distinct in view of the prior art and as would be appreciated by one of ordinary skill in the art. *Id.* Upon further consideration and in view of Applicants' disclosure that the species are not patentably distinct, the species election requirement is withdrawn.

Consequently, claims 1-6 and 16-24 are rejoined and examined on the merits.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-3, 5 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Myerholtz *et al* (US 5,306,644) ("Myerholtz").

i. Claim 1 is anticipated

Myerholtz teaches a measurement system comprising single or multiple analytes for use in a piezoelectric surface wave device, the device comprising immobilized receptor binding members specific for the analytes. *See* column 3, lines 10-14 and 28-34. In this context, the "multiple" analytes is considered to mean distinct analytes. Myerholtz also teaches that the analytes are in a liquid sample. *See* column 3, lines 44-48. Myerholtz further teaches that the analytes can be administered with "competing" receptor binding members for a competition assay. *See* column 9, lines 10-16. In this context of multiple –i.e., distinct– analytes, there are a plurality of distinct competing receptor binding members. Hence, Myerholtz teaches the situation where more than one type of receptor binding member, each type specific for a distinct analyte, is provided to the device with the analytes in a liquid sample. Consequently, Myerholtz teaches the claimed "[m]ixture of isolated or synthetic unlabelled affinity molecules in a liquid carrier comprising at least two different affinity molecules, each with affinityfor a predetermined analyte, for use in a single or multi flow cell piezoelectric crystal micro balance apparatus" recited in claim 1.

ii. Dependent claims 2-3, 5 and 16 are anticipated

Claims 2-3, 5 and 16 are dependent upon claim 1. These claims are anticipated by Myerholtz, as described above, in combination with the rationale below.

Regarding claim 2, Myerholtz teaches that the receptor binding member can form the following pairs with the analyte: antigen/antibody and complementary single stranded nucleic acid pair. *See* column 5, lines 44-51.

Regarding claim 3, Myerholtz teaches antibody fragments. *See* column 5, lines 39-40.

Regarding claim 5, Myerholtz teaches antibody in a $NaIO_4$ solution with PBS as a base. *See* column 16, lines 48-50. One of ordinary skill in the art would recognize PBS as phosphate buffer saline, which inherently contains water. The $NaIO_4$ element is considered the preservative, as claimed.

Regarding claim 16, this claim is directed to a kit. However, the only limitation in the claim is "a stable or stabilized mixture according to claim 1." Consequently, since claim 1 is taught by Myerholtz, as described above, claim 16 is correspondingly anticipated by the reference.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Myerholtz, cited above, in view of Badley *et al.* (US 6,294,391) ("Badley") (cited in the IDS filed May 22, 2006).

Myerholtz, described above, does not teach a concentration of affinity molecules between 0.01-0.8 mg/ml of the liquid carrier.

Badley teaches an immunoassay with an antibody concentration of 0.003 mg/ml. *See* column 8, lines 46-48. This concentration is taught with the analyte estriol-3-glucuronide in mind. *See* column 8, lines 41-42 and 66-67.

Given the foregoing description, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify Myerholtz's mixture of affinity molecules by placing them in solution at a concentration of 0.03 mg/ml, as taught by Badley. The reason for performing the modification would be to use a concentration capable of detecting estriol-3-glucuronide, as described by Badley. Moreover, the skilled artisan would have a reasonable expectation of success in combining the teachings of Myerholtz and Badley since the portion of Badley relied upon is one type of immunoassay that fits within Myerholtz's method.

6. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Myerholtz, cited above, in view of Strahilevitz (US 4,375,414).

Myerholtz, described above, does not teach a narcotic analyte.

Strahilevitz teaches an antibody directed at heroin, in order to detect the drug in a biological material. *See* abstract and column 1, lines 13-15.

Given the foregoing description, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the Myerholz's method by substituting an antibody directed at heroin, as taught by Strahilevitz. Such an antibody would allow a user to detect heroin in a biological material, as evidenced by Strahilevitz, thereby providing a reason for the skilled artisan to perform the stated modification.

Moreover, since Myerholtz teaches that any antibody can be used in the method, the skilled artisan would have a reasonable expectation of success in applying Strahilevitz's anti-heroin antibody to Myerholtz's method.

7. Claims 17-20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Myerholtz, described above, in view of Muldoon *et al.* (US 7,189,520) ("Muldoon").

i. Independent claim 17 is obvious

Considering the description above, Myerholtz teaches the "providing…" and "introducing a liquid sample…" steps as claimed. Myerholtz, moreover, describes the device as comprising one or more channels in a flow cassette, thereby teaching the claimed "flow cell compartments." *See* column 8, lines 52-61 and column 9, lines 29-41. Myerholtz also teaches the step of measuring shifts in resonant frequency, in order to detect mass changes on the surface of the piezoelectric device. *See* column 3, lines 4-9. Hence, Myerholtz teaches the "detecting…" step as claimed.

As described above, Myerholtz teaches a competition assay that includes an immobilized binding receptor molecule and a sample comprising an analyte and a competing binding receptor molecule. In this situation, the two binding receptor molecules compete for the analyte. However, the instant claim recites the opposite scenario in which the immobilized molecule is "at least one antigen-analogue of the predetermined analyte." Consequently, Myerholtz does not teach the "introducing the mixture…" step as claimed.

Muldoon teaches different formats for a competitive immunoassay involving an analyte and an analyte analog. *See* column 12, lines 33-55. In one format, the analyte and analog compete for an immobilized ligand. *Id.* In another format, the analyte analog is immobilized and competes with the soluble analyte for the soluble ligand. *Id.* In this context, Muldoon teaches that the immobilized ligand and immobilized analyte analog are recognized as equivalent formats for the purpose of performing a competition immunoassay. *See* MPEP 2144 for recognized equivalents described in the prior art.

Given the foregoing description, it would have been obvious to one of ordinary skill in the art to modify Myerholtz's method by replying on Muldoon to replace the immobilized binding receptor with an analyte analog. The skilled artisan would have performed the modification since Muldoon teaches that an immobilized ligand and an immobilized analyte analog are equivalent formats for performing an immunoassay. Moreover, the modification does not change the dynamics of specific binding between the binding receptor and analyte; indeed, the same concept of a competitive immunoassay applies. Accordingly, the skilled artisan would have a reasonable expectation of success in combining the teachings of Myerholtz and Muldoon.

ii. Dependent claims 18-20 and 22 are obvious

Claims 18-20 and 22 are obvious in view of the description above and in combination with the rationale below.

Regarding claims 18 and 19, Myerholtz does not describe how the sample comprising analytes are augmented with competing receptor – i.e., whether the sample

is first mixed with the competing receptor and then applied to the device, or whether the sample and competing receptor are sequentially or simultaneously applied to the device. However, the choice of one of the foregoing scenarios is limited to just four scenarios: (1) sample is mixed with the competing receptor prior to application, (2) sample is applied first and then the competing receptor, (3) competing receptor is applied first and then the sample, or (4) the sample and competing receptor are applied simultaneously to the device. In light of the fact that there are only four ways in which the sample and competing receptor can be applied, it would have been obvious to one of ordinary skill in the art to either introduce the affinity molecules to the device prior to introducing the sample (claim 18) or to mix the affinity molecules and sample prior to introducing them to the device (claim 19), as claimed. Accordingly, the instant claims are obvious over the teachings of Myerholtz.

Regarding claim 20, Myerholtz teaches antibody fragments. *See* column 5, lines 39-40.

Regarding claim 22, Myerholtz teaches antibody in a $NaIO_4$ solution with PBS as a base. *See* column 16, lines 48-50. One of ordinary skill in the art would recognize PBS as phosphate buffer saline, which inherently contains water. The $NaIO_4$ element is considered the preservative, as claimed.

8. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Myerholtz in view of Muldoon, both cited above with respect to claim 17, and further in view of Badley, also cited above.

Myerholtz and Muldoon (together "Myerholtz"), described above, do not teach a concentration of affinity molecules between 0.01-0.8 mg/ml of the liquid carrier.

Badley teaches an immunoassay with an antibody concentration of 0.003 mg/ml. *See* column 8, lines 46-48. This concentration is taught with the analyte estriol-3-glucuronide in mind. *See* column 8, lines 41-42 and 66-67.

Given the foregoing description, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify Myerholtz's mixture of affinity molecules by placing them in solution at a concentration of 0.03 mg/ml, as taught by Badley. The reason for performing the modification would be to use a concentration capable of detecting estriol-3-glucuronide, as described by Badley. Moreover, the skilled artisan would have a reasonable expectation of success in combining the teachings of Myerholtz and Badley since the portion of Badley relied upon is one type of immunoassay that fits within Myerholtz's method.

9. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Myerholtz and Muldoon, both cited above, in view of Strahilevitz (US 4,375,414).

Myerholtz and Muldoon (together "Myerholtz"), described above, do not teach a narcotic analyte.

Strahilevitz teaches an antibody directed at heroin, in order to detect the drug in a biological material. *See* abstract and column 1, lines 13-15.

Given the foregoing description, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the Myerholz's method by

substituting an antibody directed at heroin, as taught by Strahilevitz. Such an antibody would allow a user to detect heroin in a biological material, as evidenced by Strahilevitz, thereby providing a reason for the skilled artisan to perform the stated modification. Moreover, since Myerholtz teaches that any antibody can be used in the method, the skilled artisan would have a reasonable expectation of success in applying Strahilevitz's anti-heroin antibody to Myerholtz's method.

10. Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Myerholtz and Muldoon, both cited above, in view of Willner *et al* (US 7,135,295) ("Willner").

Myerholtz and Muldoon (together "Myerholtz"), described above, do not teach an explosive analyte.

Willner teaches an antibody directed at TNT for use in a piezoelectric sensor, in order to detect the presence of an explosive in certain soil samples. *See* column 3, lines 18-30 and column 5, line 66 spanning column 6, line 3.

Given the foregoing description, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the Myerholz's method by substituting an antibody directed at TNT, as taught by Willner. Such an antibody would allow a user to detect TNT samples in solid, as evidenced by Willner, thereby providing a reason for the skilled artisan to perform the stated modification. Moreover, since Myerholtz teaches that any antibody can be used in the method, the skilled artisan

would have a reasonable expectation of success in applying Willner's anti-TNT antibody to Myerholtz's method.

Conclusion

11. No claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2872. The examiner can normally be reached on Monday to Friday (8:30 am to 5:00 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon Y. Lum/
Examiner, Art Unit 1641

/Nelson Yang/
Primary Examiner, Art Unit 1641